

Bovine colostrum as a cause of hemolytic anemia in a lamb

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The syndrome of bovine colostrum-induced anemia in lambs has been reported in Europe (1,2). It is usually described in 7 to 21-day-old lambs that have been fed bovine colostrum within 6 h of birth. No breed or sex predisposition has been reported (3). In general, the signs are sudden loss of appetite and weakness affecting one or several lambs, without evidence of icterus or hemoglobinuria (3). The period from the onset of signs to death is usually less than 24 h (1–3). Immunoglobulin on the surface of red cells has been demonstrated by direct Coomb's test with antisheep immunoglobulin and anti-bovine immunoglobulin, and by direct immunofluorescence (2,5). We describe, herein, the first reported case of this condition in Canada.

A pregnant Suffolk was presented to the Large Animal Clinic of the Western College of Veterinary Medicine with a history of anorexia, weakness, and depression. Pregnancy toxemia was diagnosed, and two fetuses were removed by cesarean section. The ewe was not producing milk, so both lambs were fed bovine colostrum (2.5% body weight [BW]) via a nipple bottle q6h for the 1st day of life. Sheep milk replacer (2.5% BW) was fed q6h for the next 3 d. The twins were discharged from the clinic when 4 d old with recommendations to feed sheep milk replacer at 10% to 15% BW, q24h. The female lamb died suddenly at 6 d of age and was incinerated. No postmortem examination was performed. The male was presented at 7 d of age for evaluation of weakness, lethargy, and anorexia.

The lamb was lethargic, mildly dehydrated (6%), and weighed 6.5 kg. Rectal temperature was 38.0°C, the heart rate was 186/min, and the respiratory rate was 75/min. The sclera and oral mucous membranes were icteric. The capillary refill time was normal. No petechiae or ecchymoses were noted in the skin or mucous membranes. Thoracic and abdominal auscultation yielded normal sounds. The navel was normal and the lamb passed normal feces.

Laboratory tests showed a nonregenerative hemolytic anemia — packed cell volume (PCV) 0.06 L/L (normal, 0.24 to 0.50 L/L) — and a moderate hypoproteinemia — plasma protein 52 g/L (normal, 60 to 79 g/L). The mean corpuscular hemoglobin (12.1 pg) and mean corpuscular hemoglobin (311 g/L) concentrations were normal. Examination of stained blood films failed to show signs of immature red blood cells or eperythrozoon organisms. There was no evidence of inflammation on the complete blood count (white blood cells: $5.0 \times 10^9/L$, no band neu-

trophils, fibrinogen: 2 g/L). The blood urea nitrogen (6 mmol/L) and creatinine (65 $\mu\text{mol/L}$) concentrations were normal. Hypokalemia (3.5 mmol/L) was attributed to a combination of anorexia and low concentrations in the milk replacer. The anion gap and bicarbonate were normal. Hemoglobinuria was not observed on urinalysis. The extravascular nature of the hemolytic anemia was indicated by the presence of icteric plasma (2+), hyperbilirubinemia (73% unconjugated), and absence of hemoglobinuria.

As the anemia was life-threatening, a whole blood transfusion was given. Blood (300 mL) was withdrawn from an unrelated donor ewe into a sterile plastic collection bag containing anticoagulant (Blood pack, Baxter Corporation, Toronto, Ontario). The blood was warmed in a water bath at 40°C and administered through an in-line filter. Initially, vital parameters were recorded, and 6.6 mL of whole blood (0.1 mL/kg BW) were given over 10 min. No adverse reactions were noted and the transfusion rate was increased to 10 mL/kgBW/h. The transfused blood was not tested for compatibility with the recipient's red blood cells or serum.

Excessive hemolysis of the lamb's red cells precluded performance of a direct Coomb's test. The presence of IgG antibodies in the bovine colostrum reacting with the red cells of the lamb, blood donor, and sire, but not the red cells of the dam, were demonstrated using an indirect Coomb's test. Bovine colostrum had high titers ($>1:1024$) of IgG directed against the red cells of the lamb and its sire. Low levels of IgM antierythrocyte antibody (titers between undetectable and 1:64) were also found. Since IgG does not fix complement as efficiently as IgM, IgG-mediated hemolytic anemia usually causes extravascular hemolysis (6).

Two hours after the blood transfusion, the lamb was able to suck via a nipple bottle and could stand voluntarily. The PCV was 0.22 L/L, but it gradually decreased to 0.035 L/L by day 17 posttransfusion, when the lamb again became lethargic. Recurrence of anemia was attributed to destruction of erythrocytes by colostral antibody complexes and the lamb's mononuclear phagocytes (7). Corticosteroid therapy was not used, but could have been beneficial, since IgG antibody-mediated anemia tends to be more responsive to corticosteroids than does IgM antibody-mediated anemia (6).

On day 17, a 2nd whole blood transfusion was performed, as previously described. The dam was used as a donor because her red cells were negative in an indirect Coomb's test with the bovine colostral antibodies. Two hours after the blood transfusion, the lamb was able to nurse and stand voluntarily, the PCV was 0.22 L/L. The lamb was given 200 mg of iron (Dexafer, Austin Laboratories, Joliette, Québec), IM, to facilitate erythropoiesis. By day 30, the lamb's PCV had increased to 0.26 L/L and its total bilirubin had decreased to 10 $\mu\text{mol/L}$. Bone marrow, aspirated from the ilium on day 30, demonstrated active granulopoiesis and

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erythropoiesis with the presence of erythroid precursor cells (rubriblasts and prorubricytes). A direct Coomb's test was performed on the lamb's blood on day 30. There was no evidence of complement component C₃, or IgG or IgM antibodies bound to the lamb's erythrocytes. Indirect antiglobulin testing using the lamb's sera did not demonstrate antibodies reactive with the erythrocytes of the unrelated donor ewe, dam, or sire. Therefore, there was no evidence that the lamb had developed an immune response to the blood transfusions. The lamb was discharged on day 40 with a PCV of 0.30 L/L and a plasma protein concentration of 52 g/L. Three months after discharge, the owner reported that the lamb was in good health.

The acute onset of signs and the severe anemia made diseases caused by increased erythrocyte destruction more likely than those due to inadequate erythropoiesis. Immune-mediated hemolytic anemia may occur by two mechanisms; intravascular hemolysis, due to the fixation of complement via the classical pathway, and extravascular hemolysis with red cell destruction by phagocytosis, due to antibody-mediated opsonization of the red cells (6,8). Most hemolytic anemias are primarily caused by an increased rate of extravascular erythrocyte destruction within the mononuclear phagocytic cells of the liver and spleen (6,8). In hemolytic anemia, icterus results from increased production of bilirubin, which is a breakdown product of heme (8). Common causes of hemolytic anemia in lambs are infectious (eperythrozoonosis or leptospirosis) or immune-mediated (8). Autoimmune hemolytic anemia can occur as a primary idiopathic process, or more commonly as a secondary process (drug administration or feeding bovine colostrum to lambs). This lamb had never been treated with antibiotics or been in contact with any sources of copper. It had been fed bovine colostrum that contained antish sheep erythrocyte antibody. We believe that this lamb suffered from the syndrome of bovine colostrum-induced anemia. The sheep milk replacer, unlike the colostrum, will contain only trace amounts of immunoglobulin; therefore, it will not be capable of inducing antibody-mediated disease. The presence of antibodies to sheep blood group antigens in bovine colostrum is a common occurrence and is referred to as "heterophile antibodies." They are due to the production of antibodies to common cross-reactive antigens that are present on the surfaces of bacteria and protozoa. These epitopes are simple carbohydrate structures and are identical to the immunodominant epitopes on blood group antigens (9). With increasing use of bovine colostrum in lambs, both to prevent the spread of ovine progressive pneumonia (maedi-visna) and for other miscellaneous reasons, practitioners in North America should be aware of this syndrome.

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